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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/234,028	01/20/1999	RONALD T. RAINES	960296.95360	6579

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EXAMINER	
HUTSON, RICHARD G	
ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
01/31/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/234,028	RAINES, RONALD T.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,7,9 and 18-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,5,7,9 and 18-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/31/2007 has been entered.

Applicants cancellation of claims 2, 3, 6 and 15-17, amendment of claims 1, 4, 5, 7, 9, and the addition of new claims 18-20, in the paper of 10/31/2007, is acknowledged. Claims 1, 4, 5, 7, 9 and 18-20 are at issue and are present for examination.

Applicants' arguments filed on 10/31/2007, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4, 5, 7, 9 and 18-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection was stated in the previous office action as it applied to previous claims 1 -7, 9, 10 and 15-17. In response to the previous rejection, applicants have cancelled claims 2, 3, 6 and 15-17, amended claims 1, 4, 5, 7, 9, and added new claims 18-20 and traverse the rejection as it applies to the newly amended claims.

Applicants traverse the rejection on the basis that the rejection is moot as to cancelled Claims 2, 3, 6, 10, and 15-17 and request reconsideration of the rejection of Claims 1, 4, 5, 7 and 9 is respectfully requested in view of the aforementioned amendments to Claim 1.

Applicants complete amendment of the claims is acknowledged, however, continues to be insufficient to overcome the current rejection because applicant's amendment continues to describe the native RI or RIs from which the variant RIs are generated, and not the claimed variant RIs themselves.

Applicant's amendments to the claims continue to be directed to the "means by which" the final product is obtained, rather then to the actual final claimed product (i.e. the ribonuclease inhibitor variant or mutant). As these means or processes do not place limitations on the final claimed product, by virtue of applicant's recitation "the difference consists of at least one...", applicants still have not t limited the scope of the

claimed product and the scope of the claimed product continues to not be adequately described for the reasons previously stated.

Applicants continue to be reminded that while applicants specification provides two examples of ribonuclease inhibitors variants that could be the result of those "process limitations" required by the claims, two species is not sufficient to adequately describe the genus of claims which includes any and all such ribonuclease inhibitor variants. The specification also fails to describe additional representative species of these ribonuclease inhibitor variants by sufficient structural characteristics or properties other than the activities recited in claim 1 and the disclosed cysteine modifications, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1, 4, 5, 7, 9 and 18-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a mutant ribonuclease inhibitor comprising the amino acid sequence of SEQ ID NO: 3, wherein said mutation is a substitution in one of its two adjacent cysteine residues to an amino acid residue not

capable of forming a disulfide bond, the mutant ribonuclease inhibitor having a greater resistance to oxidation, the mutant ribonuclease inhibitor retaining its specificity and binding affinity to ribonuclease, does not reasonably provide enablement for any variant ribonuclease inhibitor differing from references SEQ ID NO: 3 or 2 wherein the difference consists of at least one of the residues at positions 95, 96, 329 and 330, relative to SEQ ID NO: 3 and wherein the difference consists of at least one of the residues at positions 324and 3250, relative to SEQ ID NO: 2 being an alanine, the mutant ribonuclease inhibitor having a greater resistance to oxidation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection was stated in the previous office action as it applied to previous claims 1-7, 9, 10 and 15-17. In response to the previous rejection, applicants have cancelled claims 2, 3, 6 and 15-17, amended claims 1, 4, 5, 7, 9, and added new claims 18-20 and traverse the rejection as it applies to the newly amended claims.

Applicants traverse the rejection on the basis that the rejection is moot as to cancelled Claims 2, 3, 6, 10, and 15-17 and request reconsideration of the rejection of Claims 1, 4, 5, 7 and 9 is respectfully requested in view of the aforementioned amendments to Claim 1

Applicants traverse the rejection on the basis that the rejection is moot as to cancelled claims 2, 3, 6, 10, 15 and 17 and applicants request reconsideration of the

rejection of Claims 1, 4, 5, 7, and 9 in view of the aforementioned amendments which refer specifically and unambiguously to the structures of claimed variants.

As above, applicants complete argument and amendments are acknowledged and have been carefully considered, however, continue to be found non-persuasive for the reasons previously made of record and for those repeated herein. Applicant's amendment and supporting argument is not persuasive because applicant's amendment continues to describe the native RI or RIs from which the variant RIs are generated, and not the claimed variant RIs themselves.

As stated above, applicant's arguments continue to be along the same principal of reason previously presented. Applicants referred to changes to the claim continue to be directed to the "means by which" the final product is obtained, rather then to the actual final claimed product (i.e. the ribonuclease inhibitor variant or mutant). As these means or processes do not place limitations on the final claimed product, it continues that applicants have not thus limited the scope of the claimed product and the scope of the claimed product continues to not be enabled for the reasons previously stated.

With respect to the enablement of the claimed genus, applicants specification does not support the broad scope of the claims which encompass all modifications and fragments of any mutant ribonuclease which does not comprise said cysteine mutations because the specification does not establish: (A) regions of the protein structure which may be modified without effecting ribonuclease inhibitor activity and oxidative resistance; (B) the general tolerance of ribonuclease to modification and extent of such

tolerance; (C) a rational and predictable scheme for modifying any amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

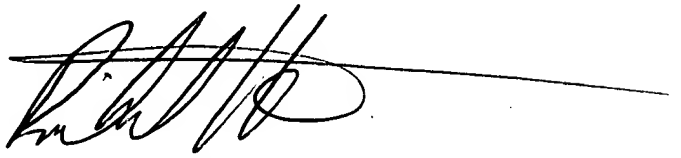
Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of any ribonuclease inhibitor. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those mutants having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

The rejection of claims 1-7, 9, 10, 15 and 17 under 35 U.S.C. 102(b) as being anticipated by Blazquez et al. (Journal of Biological Chemistry, Vol 271, pp 18638-18642, 1996) is hereby withdrawn based upon applicants amendment of the claims that requires that the claimed ribonuclease inhibitor consists of at least an alanine at positions 95, 96, 329 and 330 of reference SEQ ID NO: 3 or applicants amendment of the claims that requires that the claimed ribonuclease inhibitor consists of at least an alanine at positions 324 and 325 of reference SEQ ID NO: 2.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
1/29/2007